



RESEARCH ARTICLE

ROLE OF HEMATOLOGICAL SCORING SYSTEM IN DIAGNOSIS OF NEONATAL SEPSIS

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Abstract

Introduction: Neonatal sepsis is a clinical syndrome resulting from pathophysiologic effects of local and systemic infection in the 1st month of life. Septicemia usually consists of bacteremia with a constellation of signs and symptoms caused by microorganisms or their toxic products in the circulation. Neonatal sepsis was one of the common causes of neonatal mortality, contributing to 16% of all intramural deaths. Early diagnosis of neonatal septicemia is a vexing problem because of its nonspecific clinical picture.

Method: This study was prospective observational study of 210 Cases received from August 2020 to August 2022 for Neonatal Sepsis. This prospective study was carried out in Department of Pathology of a tertiary care teaching hospital. The ethical permission has been obtained from Institutional Ethics Committee for conducting the study. Hemogram was obtained for each case using five part automated hematology analyser.

Result: Hematological scoring system was useful test in the early diagnosis of neonatal sepsis. Diagnostic accuracy was 92.39% in this study, ≥ 3 score was sensitive and ≥ 4 score was specific for early diagnosis of neonatal sepsis

Conclusion: The HSS increases the diagnostic accuracy of the complete blood cell count as a screening test for sepsis and simplifies and standardizes its interpretation.

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Introduction:-

Neonatal sepsis is a clinical syndrome resulting from pathophysiologic effects of local and systemic infection in the 1st month of life. Septicemia usually consists of bacteremia with a constellation of signs and symptoms caused by microorganisms or their toxic products in the circulation. (1) The infection can be contracted from the mother through transplacental route, ascending infection, during passage through an infected birth canal, or exposure to infected blood at delivery. (2) The newborn infants are more prone to bacterial invasion than the older children or adults, due to their weaker immune system, premature babies being even more susceptible. Neonatal sepsis was one of the common causes of neonatal mortality, contributing to 16% of all intramural deaths. (3) Early diagnosis of neonatal septicemia is a vexing problem because of its nonspecific clinical picture. (4) Hence the timely diagnosis of

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sepsis in neonates is critical as the illness can be rapidly progressive and, in some instances, fatal. (5) Although blood culture is considered to be the gold standard for diagnosis of septicemia, the technique is time consuming and demands a well-equipped laboratory, which is not available in most of the community hospitals. Various studies have shown that hematological parameters are simple, quick, and cost-effective tools in the early diagnosis of neonatal sepsis. They are also useful early predictors of neonatal septicemia; thus helping to initiate early treatment with appropriate antibiotics. (6) Here, in this study, we evaluate the performance of the hematological scoring system (HSS) of Rodwell et al. (7) in 210 neonates for the early detection of sepsis in high-risk infants, which should improve the diagnostic accuracy of the complete blood cell count as a screening test. The present study is undertaken to evaluate the utility of the HSS in the early diagnosis of neonatal sepsis.

Method:-

This study was prospective observational study of 210 Cases received from August 2020 to August 2022 for Neonatal Sepsis. This prospective study was carried out in Department of Pathology of a tertiary care teaching hospital. The ethical permission has been obtained from Institutional Ethics Committee for conducting the study. Blood was drawn from all study subjects under aseptic precautions in EDTA vacutainer. Hemogram was obtained for each case using five part automated hematology analyser. Blood films are often prepared from samples of Ethylene diamino tetra acetic acid (EDTA) anticoagulated blood or non-anticoagulated blood (fingerprick procedure).

Inclusion criteria:-

Neonates (first 28 days of life) with clinical signs and symptoms of Neonatal Sepsis as per mention in laboratory request form.

Exclusion criteria:-

1. Patients with more than 28 days of life.
2. Neonates who doesn't have signs and symptoms of Neonatal Sepsis.

Data analysis:

Descriptive and analytic analysis of data was done with Microsoft excel. Peripheral blood smear was then prepared immediately, stained with Leishman stain/Geimsa stain and examined. Hematological scoring system of Rodwell et al. (7) HSS assigns a score of 1 for each of seven findings significantly associated with sepsis.

Table I:- Haematological scoring system.

No	Criteria	Abnormality	Score
1	Total Leucocyte count (cells/cumm)	$\leq 5000/\text{mm}^3$ $\geq 25,000 \text{ mm}^3$ at birth $\geq 30,000 \text{ mm}^3$ after 12-48h $\geq 21,000 \text{ mm}^3$ day 2 onwards	1
2	Total PMN count	No mature PMN seen $\downarrow$ or $\uparrow$	2 1
3	Immature neutrophil count (cells/cumm) I:T I:M	≥ 0.2 ≥ 0.3	1 1
4	Degenerative changes in Neutrophils	Toxic granules/cytoplasmic vacuoles	1
5	Platelet count	$< 1,50,000/\text{mm}^3$	1

I: T – Immature to total neutrophils ratio; I:M – Immature to mature neutrophils ratio; ANC – Absolute neutrophil count

ESR (Erythrocyte Sedimentation Rate): ESR done in semi automated ESR analyzer and manually by Westergren method.

Statistical Analysis

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of HSS, relative to cultural positivity were analysed.

The data presented as number and percentages for the qualitative data. Chi-square test was used in the comparison between two groups with qualitative data. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value considered significant as the following: $P > 0.05$: Non-significant (NS)

$P < 0.05$: Significant (S) $P < 0.01$: Highly significant (HS)

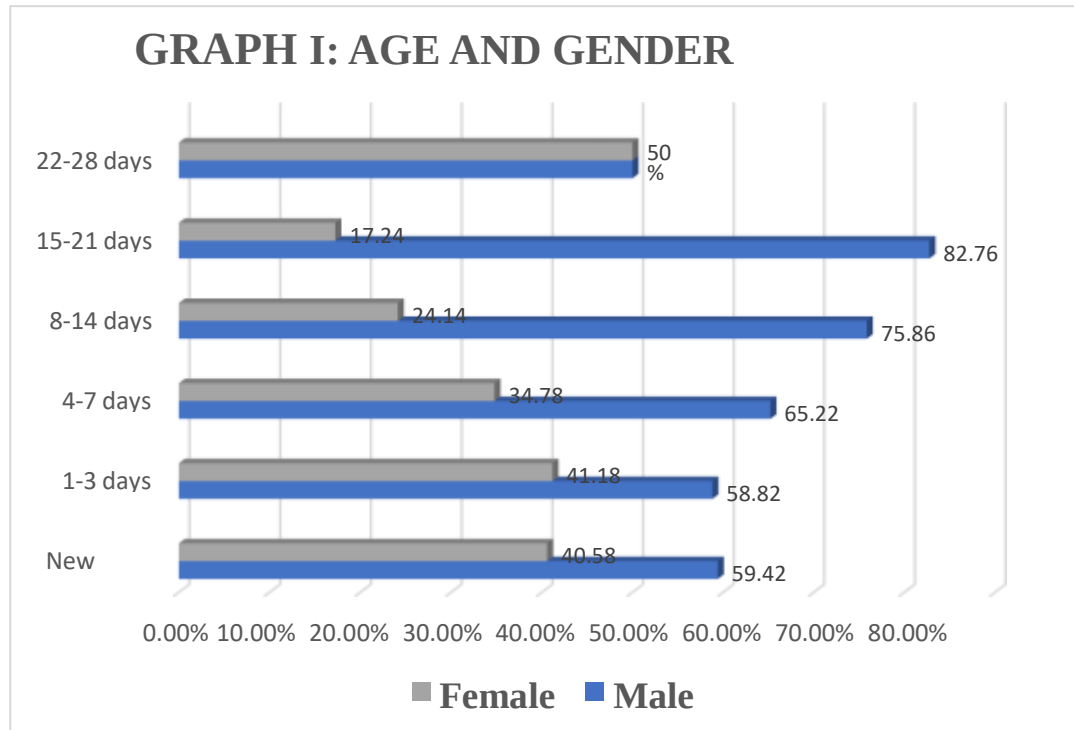
Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of HSS, relative to cultural positivity were analyzed.

1. True positive (TP): Variation in hematological parameters according to HSS and presence of organism confirmed in the Blood culture.
2. False positive (FP): Variation in hematological parameters according to HSS, but no organism in the Blood culture.
3. True negative (TN): No variation in hematological parameters according to HSS, no organism in the Blood culture.
4. False negative (FN): No variation in hematological parameters according to HSS, but presence of organism in the Blood culture.
5. Sensitivity (S): Proportion of patients with associated Neonatal sepsis and a positive result in hematological parameter according to HSS, $S = TP / (TP + FN)$
6. Specificity (Sp): Proportion of patients without associated Neonatal sepsis and with a negative result in hematological parameter according to HSS $= TN / (FP + TN)$.
7. Positive predictive value (PPV): Proportion of patients with a positive result and blood culture confirmation of PPV $= TP / (TP + FP)$
8. Negative Predictive value (NPV): Proportion of patients with negative results, without Neonatal sepsis in the blood culture. NPV $= TN / (TN + FN)$

Result:-

Out of 210 neonates, 135 (64.29%) were male and 75 (35.71%) were female. The Incidence of Neonatal sepsis was more common in male than women. Out of 210 cases, 106 neonates had early onset type sepsis and 104 neonates had late onset type of sepsis. Diagnostic accuracy of HSS was 92.39%. P value was 0.002 with comparison with blood culture report which was significant.

$HSS \geq 1$ could be used for the early diagnosis of Neonatal Sepsis

**Table II:-** Hematological Parameters Of Sepsis.

Hematological parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Total leucocyte count	85.19%	88.09%	95.83%	61.67%
Total PMN count	50%	48.88%	72.63%	24.17%
Immature neutrophil count	71.43%	50%	83.33%	33.33%
I:T PMN ratio	16.67%	50%	50%	16.67%
I:M PMN ratio	16.67%	50%	50%	16.67%
Degenerative changes in Neutrophils	26.27%	87.5%	92.30%%	17.21%
Platelets count	66.90%	71.11%	87.73%	41.02%

Table III:- Hematological Scoring System Comparison With Blood Culture.

Hematological Scoring system	Culture Positive	Culture Negative	Total
0-2	100	43	143
3-4	36	1	37
>=5	4	1	5
Total	140	45	185

Chi-Square=12.012, P=0.002

Chi-square applied for measuring P value. P value was 0.002 which was significant.

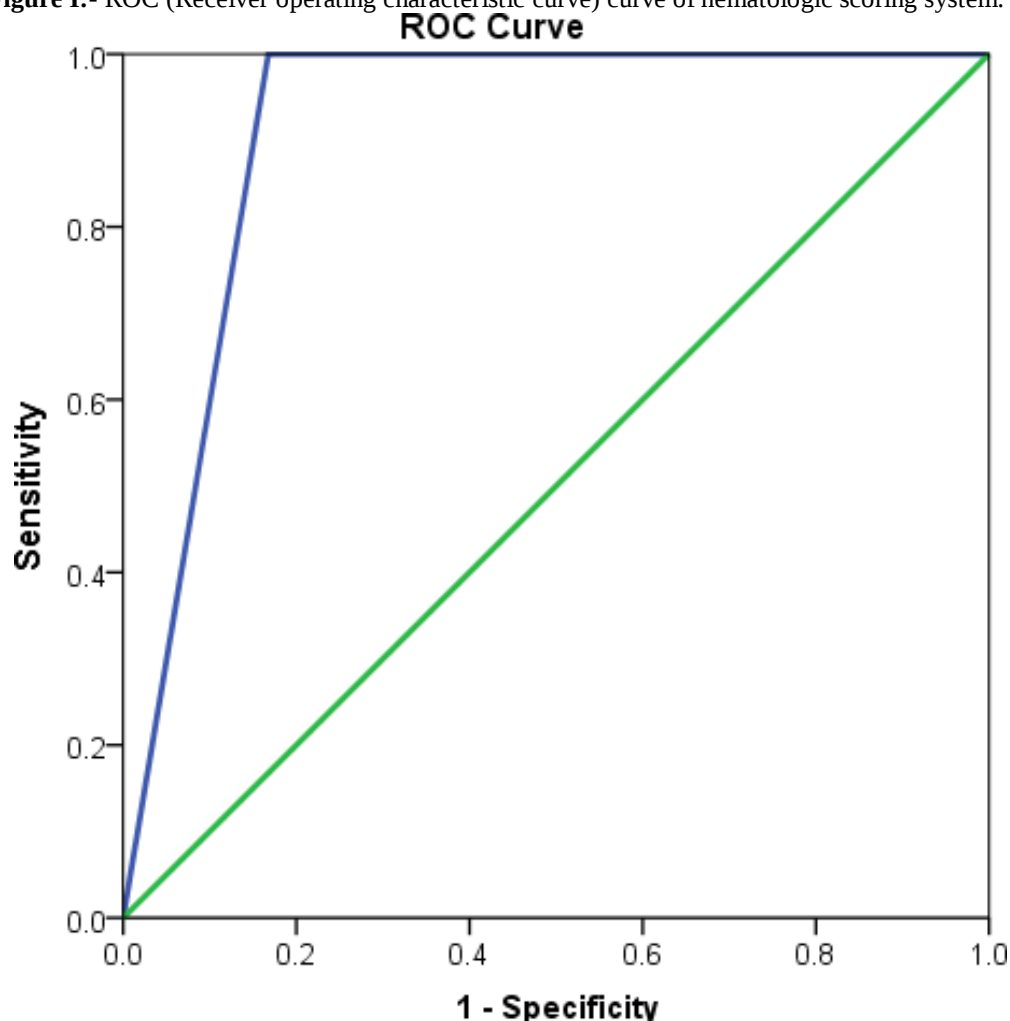
Table IV:- Hematological Scoring System According Low To High Score.

HSS	Sensitivity (%)	Specificity (%)	Positive Predictive value(%)	Negative Predictive value (%)
>=1	98.56	35.55	82.53	88.89
>=2	73.33	91.67	91.94	94.28

≥ 3	95.12	89.19	95.12	94.27
≥ 4	75	97.05	85.71	94.27
≥ 5	60	97.05	75	94.28

Table V:- Analysis Of Statistics For Hematological Scoring System As Diagnostic Test For Neonatal.

Cut off values	SN%	SP%	PPV%	NPV%	Accuracy%
HSS	73.33	91.67	91.94	94.28	92.39

Figure I:- ROC (Receiver operating characteristic curve) curve of hematologic scoring system.**Table VI:-** Area Under The Curve.

Test Result Variable: Blood Culture				
Area	SE ^a	P value ^b	Asymptotic 95% CI	
			Lower Bound	Upper Bound
0.916	0.021	0.000	0.875	0.957
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

SE: Standard error

CI: Confidence Interval

ROC: Receiver operating characteristic curve

HSS ≥ 1 could be used for the early diagnosis of Neonatal Sepsis

Table VII:- Hematological Scoring System Comparison With ESR.

Hematological Scoring system	ESR (0 to 2 mm/hr)	ESR (>2mm/hr)	Total
0-2	28	154	182
3-4	6	18	24
>=5	1	3	4
Total	35	175	210

Discussion:-

The early diagnosis of neonatal septicemia is primarily based on clinical evaluation but laboratory diagnosis requires a microbiologic-clinical correlation. Many neonates were treated empirically with antibiotics for several days while waiting for bacteriologic culture for suspected infection.⁽⁸⁾ The gold standard for diagnosis of neonatal sepsis is a positive blood culture which requires a minimum period of 48-72 hours.⁽⁹⁾

The current study was undertaken to evaluate haematological scoring system of neonatal septicemia and to look into various hematological parameters both individually and in combination as part of sepsis screening.

The current study was undertaken to evaluate haematological scoring system of neonatal septicaemia and to look into various haematological parameters both individually and in combination as part of sepsis screening.

In Present study, Male is most commonly affected in 15-21 days age group where Female is most commonly affected in 22-28 days age group. Rekha N.⁽⁹⁾ study found, 22-28 days most common affected age group in Male and 1-3 days most common affected in female.

In present study, Highest sensitivity seen in Total leucocyte count 85.19%, study done by Derbala SG et al.⁽¹⁰⁾ study sensitivity was 90% which is concordance with our study where study done by Aparna S⁽¹¹⁾, Khair KB et al.⁽⁸⁾, Rodwell et al.⁽⁷⁾ are discordance with our study. This variation is seen may due to sample size.

In present study, Highest specificity seen in Total leucocyte count 88.09%, study done by Derbala SG et al.⁽¹⁰⁾ study specificity was 93.3%, study done by Aparna S⁽¹¹⁾ was 91.66%, study done by Khair KB et al.⁽⁸⁾ was 91.66% which are concordance with our study. Study done by Rodwell et al.⁽⁷⁾ was 92% which was concordance with our study. In present study, Highest sensitivity seen in >=3 which was 95.12%, study done by Rodwell et al.⁽⁷⁾ Meirina F⁽¹²⁾, Khair KB et al.⁽⁸⁾ were 96% 100% and 100% respectively which are concordance with our study. In present study, Highest specificity seen in >=4 and >=5 which was 97.05% and 97.05% respectively, study done by Meirina F⁽¹²⁾ was 90% for >=4 and which is concordance when, Khair KB et al.⁽⁸⁾ was 60% for >=4 which is discordance with our study. When study done by Meirina F⁽¹²⁾ was 96.7% for >=5 and Khair KB et al. was 87% which are concordance with our study. Study done by Rodwell et al.⁽⁷⁾ was 96% for >=5 and 89% for >=4 which was concordance with our study.

Table VIII:- Comparison Of HSS By Statistical Parameters.

Statistical Parameters	Hematological Scoring System				
	Munazza Saleemet et al. study(2014) ⁽¹³⁾	Pramana KP et al. study(2016) ⁽¹⁴⁾	Derbala SG et al. study(2017) ⁽¹⁰⁾	Elsayed et al. study(2021) ⁽¹⁵⁾	Present Study
Sensitivity	90%	80.9%	95%	96%	73.33%
Specificity	74.5%	92.7%	96.7%	90%	91.67%
PPV	65.9%	85%	26%	86.7%	91.94%
NPV	93.2%	90.5%	100%	86%	94.28%
Diagnostic Accuracy			95.5%		92.39%

Table IX:- Comparison Of Area Under Curve In Neonatal Sepsis.

Area Under curve			
DerbalaSG et al.study (2017) ⁽¹⁰⁾	Elsayed et al.study(2021) ⁽¹⁵⁾	Jacob SJ et al.study(2018) ⁽¹⁶⁾	Present study
0.954	0.76	0.90	0.916

Conclusion:-

The HSS increases the diagnostic accuracy of the complete blood cell count as a screening test for sepsis and simplifies as well as standardizes its interpretation. P value for HSS as compared with culture was 0.002 which was highly significant. Blood culture which is gold standard for diagnosis is difficult to obtain and has a very low sensitivity due to various preanalytical and analytical issues and which requires a minimum period of 48-72 hours.

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